UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,304	02/21/2001	Christopher Silvia	018512-00041	3840

7590 06/16/2003

Annette Parent
Townsend & Townsend & Crew
8th Floor
Two Embarcadero Center
San Francisco, CA 94111-3834

EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/623,304	SILVIA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 04 March 2003 (Paper No. 19) has been entered in full. Claims 1 and 6 are amended and claims 5 and 8-35 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4 and 6-7 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 3-4 of the previous Office Action (Paper No. 16, 23 October 2002) are *withdrawn* in view of the amended specification and title (Paper No. 19, 04 March 2003).

2. The rejection to claims 1-7 and 9 under 35 U.S.C. 112, first paragraph, enablement (for recitation of percent identity) as set forth at pg 8-11 of the previous Office Action (Paper No. 16, 23 October 2002) is *withdrawn in part* in view of the amended claims (Paper No. 19, 04 March 2003). Please see section on 35 U.S.C. 112, first paragraph below.

3. The rejection to claims 1-7 and 9 under 35 U.S.C. § 112, first paragraph, written description, as set forth at pg 11-13 of the previous Office Action (Paper No. 16, 23 October 2002) is *withdrawn* in view of the amended claims (Paper No. 19, 04 March 2003).

4. The rejections to claims 5-6 and 8-9 under 35 U.S.C. § 112, second paragraph, as set forth at pg 13 of the previous Office Action (Paper No. 16, 23 October 2002) are *withdrawn in part* in view of the amended and cancelled claims (Paper No. 19, 04 March 2003). Please see section on 35 U.S.C. § 112, second paragraph, below.

5. The supplemental information disclosure statement filed on 04 March 2003 (Paper No. 18) has been considered.

Claim Rejections - 35 USC § 101 and 35 U.S.C. § 112, first paragraph

6. Claims 1-4 and 6-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for originally filed claims 1-9 at pg 4-7 of the previous Office Action (Paper No. 16, 23 October 2002).

Specifically, claims 1-4 and 6-7 are directed to an isolated nucleic acid encoding a polypeptide monomer comprising an alpha subunit of a potassium channel, the polypeptide monomer (i) forming with at least one additional Kir alpha subunit, a potassium channel having the characteristic of inward rectification, (ii) encoded by a nucleic acid molecule that selectively hybridizes under highly stringent hybridization conditions to a nucleotide sequence of SEQ ID NO: 2. The claims also recite a nucleic acid that encodes human Kir5.1, a nucleic acid that encodes SEQ ID NO:1, and a nucleic acid that has a nucleotide sequence of SEQ ID NO: 2. The claims recite that the nucleic acid encodes a polypeptide monomer having a molecular weight of about between 38kDa to 48kDa, wherein the molecular weight is predicted based on amino acid sequence.

Applicant's arguments (Paper No. 19, 04 March 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that after reading the present specification, the skilled practitioner would appreciate that the Kir 5.1 channel to be an inward rectifying potassium channel useful for

modulating cell excitability and membrane potential. Applicant argues that in Example 1 of the specification, human Kir5.1 is expressed according to standard methodology in cells and that the claimed nucleic acids encode an inward rectifying potassium channel. Applicant also contends that Figure 2 demonstrates that Kir5.1 is widely expressed in different cell types. Applicant submits that the claimed nucleic acids encode an inwardly rectifying potassium channel useful for modulating cell excitability. Applicant also indicates that because the Kir5.1 channel is capable of modulating cell excitability, the Kir5.1 channel is a useful target for the treatment of diseases and conditions caused by altered neuronal cell excitability. Applicant argues that the targeting of Kir5.1 is an appropriate strategy for modulating cell excitability and resting potential without respect to the original cause of the condition.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action (Paper No. 16, 23 October 2002), the asserted utility of Kir5.1 as an inwardly rectifying potassium channel to modulate cell excitability and membrane potential is credible, but not specific or substantial. The specification does disclose that 1:1 mixtures of hKir5.1 and hKir4.1 or cells expressing a tandem dimer of hKir5.1 and hKir4.1 show greater fluorescent dye changes than do cells expressing hKir5.1 (pg 57, Figure 1).). However, the specification does not disclose an absolute negative control wherein the sample cells do not contain either Kir5.1 or Kir4.1. It cannot be determined from Figure 1 if the cells expressing hKir5.1 alone would have a current magnitude significantly larger than control cells not expressing the channel. Although this asserted utility is credible, it is not specific because such assays can be performed with any polypeptide. Furthermore, since the skilled artisan would not readily use the claimed polypeptide to form a heteromeric potassium channel because the protein

has not been shown to have an increased current magnitude compared to control, the asserted utility is not substantial. It is noted that Applicant is encouraged to submit any pre- or post-filing date references or evidence in the form of a declaration under 37 C.F.R. 1.132 to support the specification.

The asserted utility of tissue typing for the claimed hKir5.1 is credible, but not specific or substantial. The specification of the instant application teaches that hKir5.1 is expressed in various tissues, including pancreas, thyroid gland, salivary gland, and kidney (pg 58). However, the asserted utility of tissue typing for hKir5.1 is not substantial because one skilled in the art would not readily use the protein in tissue-typing in a real world sense since the protein is not specific to one tissue and is not associated with any disease or disorder. Furthermore, this asserted utility is not specific because numerous unrelated proteins would also show a similar tissue typing pattern. Also, evidence of mere expression in a tissue is not tantamount to a showing of a role in hypertension, acute renal failure, chronic renal failure, diabetes insipidus, diabetic nephropathy, hypothyroidism, hyperthyroidism, goiter, hypoparathyroidism, hyperparathyroidism, pancreatic insufficiency, diabetes, cystic fibrosis, sialorrhea, and salivary insufficiency.

Furthermore, the asserted utility of using the Kir5.1 channel as a target for the treatment of diseases and conditions caused by altered neuronal and cell excitability is credible, but not specific or substantial. The specification discloses nothing about the normal levels of expression of the polynucleotide. The specification also does not disclose disorders or conditions *associated* with the Kir5.1 gene, either normal or mutated/deleted/translocated. Significant further experimentation would be required of the skilled artisan to identify individuals with such a

disease or condition. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

(ii) Applicant asserts that the present application provides sequences encoding a Kir5.1 channel and methods for modulating a Kir5.1 channel. Applicant states that agonists and antagonists of Kir5.1 can routinely be identified by applying compounds to Kir5.1-expressing cell. Applicant argues that after reading the present application, the skilled practitioner would know how to identify Kir5.1 channel agonists and antagonists useful for modulating cell excitability.

Applicant's arguments have been fully considered but are not found to be persuasive. The asserted utility of using the Kir5.1 channel to identify agonists and antagonists is credible but not specific or substantial. Such assays can be performed with any polynucleotide or polypeptide, as evidence by the general screening methods at pg 40-44 of the specification. However, the specification discloses nothing specific or substantial for the agonists and antagonists that can be identified by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

7. Claims 1-4 and 6-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not

know how to use the claimed invention. The basis for this rejection is set forth at pg 7-8 of the previous Office Action (Paper No. 16, 23 October 2002).

Applicant's arguments (Paper No. 19, 04 March 2003), as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the above-mentioned reasons.

Applicant argues that a real world utility is established and therefore, the enablement rejection associated with the lack of utility is traversed. Essentially, Applicant argues that the specification contains ample directions to practice the invention, such as methods of cloning human Kir5.1 nucleic acid sequences, immunological detection of hKir5.1 polypeptides, and assays for activity of an inward rectifier potassium channel and modulators of hKir5.1, among others.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, since Applicant has not provided evidence to demonstrate that the hKir5.1 polynucleotide and polypeptide have a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

8. Claims 1-4 and 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Stringency is relative, and the art does not recognize a single set of conditions as stringent. The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions (e.g., "hybridizes at wash conditions of

A X·SSC and **B** % SDS at **C**°C"), claims 1-4 and 6-7 fail to define the metes and bounds of the varying structures of polynucleotides recited.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant asserts that the present amendment to claim 1 adds the recitation of specific hybridization conditions for both "stringent" and "moderately stringent" hybridization conditions.

Applicant's arguments have been fully considered but are not found to be persuasive. The term "comprising" encompass various unknown stringency conditions, which would allow for the stringency to be lowered before the hybridization is ended, thereby producing polynucleotide variants other than that of hKir5.1. (Please note that this issue could be overcome by amending the claims to recite "consisting of" rather than "comprising".)

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
June 9, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER